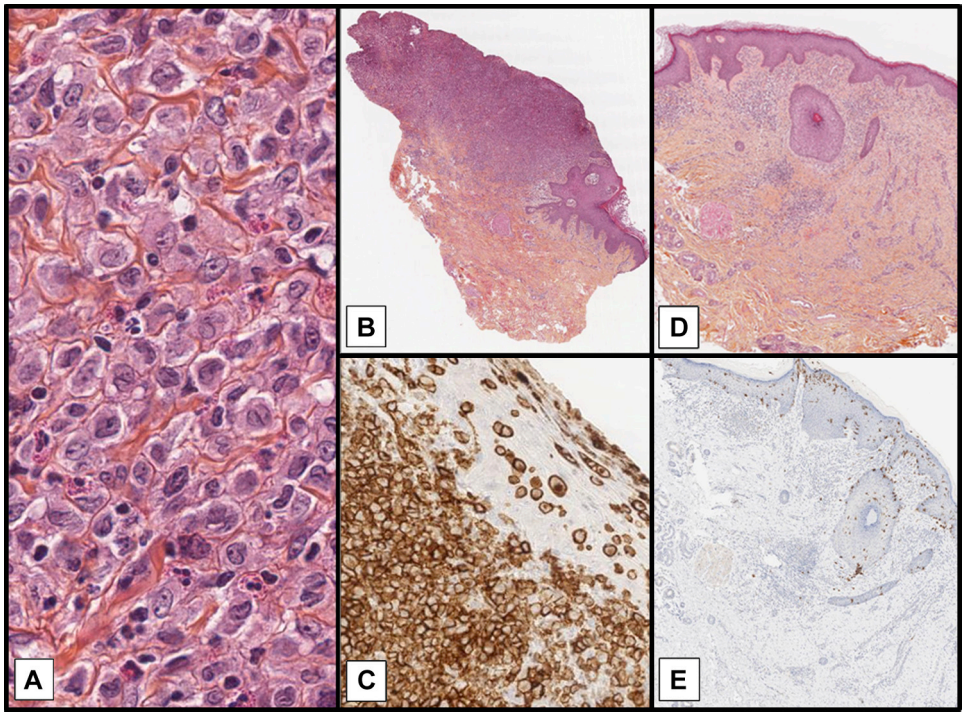

Fig 2. Histologic and immunohistologic pictures of Langerhans cell histiocytosis. **A**, Histologically, tumor cells were medium-sized, with grooved or indented nuclei and abundant eosinophilic cytoplasms. Moderate cellular pleomorphism was also a feature. Mitoses were not exceptional, with absence of overtly atypical forms. **B**, Low-power view of the biopsy specimen before treatment. **C**, Tumor cells were uniformly stained by the CD1a antibody, which also highlighted epidermotropic tumor cells. **D**, After 3 weeks of vemurafenib treatment, the dermal infiltrate had entirely disappeared, being replaced by mixed inflammatory cells. **E**, After treatment, immunostaining for CD1a was restricted to skin-resident Langerhans cells. (**A**, **B**, and **D**, Hematoxylin-eosin stain; original magnifications: **A**, ×40; **B**, ×2.5; **D**, ×2.5. **C** and **E**, SABC; original magnifications: **C**, ×10; **E**, ×5.)

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Extensive scleredema adultorum with loss of eccrine glands

To the Editor: Scleredema adultorum is a disease characterized by woody induration of the skin,[1] in which the skin appendages are usually preserved. Here, we report a case of scleredema adultorum with loss of eccrine glands leading to frequent heat strokes.

A 50-year-old Taiwanese woman visited us for hardened and thickened skin extending from the nape to the lower aspect of her back over the past 5 years. Her back became anhidrotic and the front of her trunk seemed hyperhidrotic. In the meantime, she became progressively intolerant to heat and experienced several episodes of heat strokes. She refrained from outdoor activities to avoid heat strokes. She had a 20-year history of type 2 diabetes mellitus under insulin treatment over the past 10 years. She denied previous radiotherapy, topical medications, toxin exposure, or family history of similar skin changes. Neither photosensitivity nor arthritis was present.

Examination revealed the skin from her nape to the lower aspect of her back was hardened and thickened, except the side aspects. The overlying skin was slightly erythematous with preservation of the hair follicles. Starch-iodine test showed the lesional skin was anhidrotic (Fig 1). Her blood tests were negative for antinuclear antibody, anti-Scl-70 antibody, and rheumatoid factor and pulmonary function test result was within normal limits. Fasting glucose level was 234 mg/dL and hemoglobin A1c (HbA1c) was 9.6%.

Fig 1. Scleredema adultorum. Erythematous plaque extending from her nape to the lower aspect of her back (*left*) with anhidrosis on starch-iodine test (*right*).

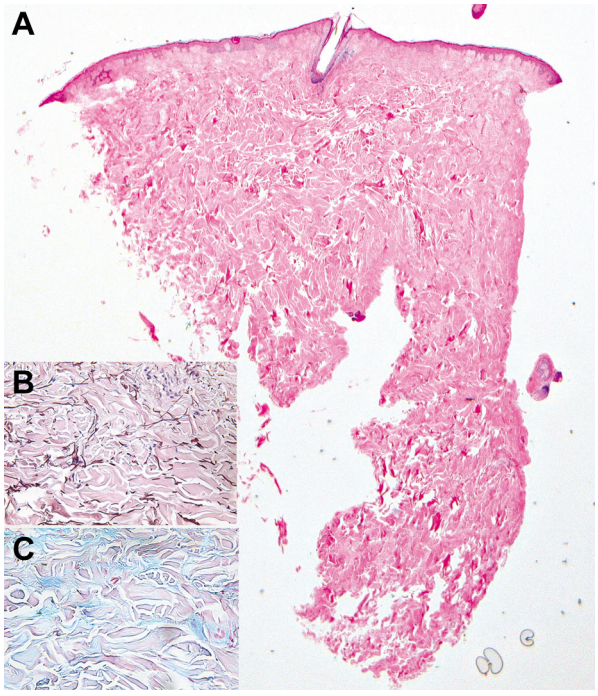

Fig 2. Scleredema adultorum histopathology. **A**, Dermal sclerosis with loss of eccrine glands and slight focal lymphocytic infiltrate around hair follicles; **B** and **C**, increased mucin deposition and decreased elastic fibers (*inset*). (Hematoxylin-eosin stain; original magnification: ×25. Inset, orcein [**B**] and alcian blue [**C**] stains; original magnification: ×40.)

The skin biopsy specimen showed markedly thickened dermis with increased collagen deposition, increased mucin, and decreased elastic fibers (Fig 2). Direct immunofluorescence was negative for IgG, IgA, IgM, complement component 3 (C3), fibrinogen, and complement component 1, q subcomponent (C1q). Although scleromyxedema cannot be ruled out by pathology findings, clinical presentations and history above favored scleredema adultorum associated with long-term diabetes. Eccrine glands were absent in serial sections (Fig 2), which explained her anhidrosis clinically. Neither squamatization nor perieccrine inflammation was noted. She was treated with oral allopurinol (100 mg/d).[2] After 8-month follow-up, the erythema and induration were slightly lessened, but the anhidrosis persisted.

Scleredema adultorum is divided into 3 distinct types that are associated with preceding infection, paraproteinemia, and diabetes mellitus, respectively.[1] In cases associated with infection, the disease onset is more abrupt and the skin hardening can usually regress. However, scleredema in diabetic patients, like our case, progresses slowly and the condition persists.

The association with loss of eccrine glands is a distinct finding in our patient. Several diseases can lead to hardened skin with loss of skin appendages, including systemic sclerosis, lupus erythematosus, radiotherapy, and chronic graft-versus-host disease.[3-5] One hypothesis is that cells in the eccrine glands are converted to myofibroblasts through epithelial-mesenchymal transition and promote fibrosis.[4] There were no signs of autoimmune diseases in this patient, such as Raynaud phenomenon, dysphagia, myopathy, or difficulty breathing, nor did the clinical presentation support such diagnoses.

In reviewing 22 cases of scleredema adultorum at our hospital from 2000 to 2012, we found no similar changes of eccrine loss pathologically. How the eccrine glands were lost in this case is unknown. We noted a slight mononuclear infiltrate around the preserved hair follicles histologically. The complete loss of eccrine glands hinders further determination of whether eccrine glands were destroyed by preceding inflammatory infiltrate.

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Conflicts of interest: None declared.

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Papular eruption associated with palifermin

To the Editor: A 52-year-old man with nasal-type extranodal natural killer T-cell lymphoma presented with a 2-day history of scattered faintly erythematous and skin-colored papules on the back of the neck and bilateral upper extremities. He noted mild pruritus associated with these lesions. Three days before the eruption, the patient began treatment as an inpatient with palifermin as mucositis prophylaxis for chemotherapy and autologous stem cell transplantation. Physical examination was notable for scattered flat-topped erythematous papules on the back of the neck, back of the hands, and forearms (Fig 1). Examination of the oral mucosa was unremarkable. A shave biopsy specimen obtained from the back of the left hand (Fig 2) revealed a slightly mamillated epidermis with acanthosis, hypergranulosis, and mild keratinocytic atypia of the basal and lower spinous layers. The patient was given the diagnosis of a palifermin-associated papular eruption and was given triamcinolone acetonide for relief of pruritus.

Palifermin is a recombinant, N-truncated version of human keratinocyte growth factor with similar binding properties but increased stability. It is Food and Drug Administration approved for reducing the incidence and duration of severe oral mucositis in patients with hematologic malignancies receiving chemotherapy, radiotherapy, and hematopoietic stem cell transplantation.[1] Palifermin is administered intravenously at a dose of 60 μg/kg/d for 3 consecutive days before radiation therapy and 3 consecutive days after stem cell transplantation.[1] The average cost of palifermin for a 70-kg patient is approximately $10,000.[1] Adverse cutaneous reactions to palifermin in early clinical trials were described as "rash," "erythema," or "pruritus" and were noted in 55%, 44%, and 50% of treated patients, respectively.[1,2] Other mucocutaneous reactions, including thickening and whitening of the tongue, oral and flexural hyperpigmentation or erythema, acanthosis nigricans–like eruptions, palmoplantar erythrodysesthesia, and intertriginous papular eruptions have since been described in the literature.[2-6]

Our patient's presentation most closely resembles cases of flexural lichenoid or verruca plana–like papular eruptions associated with palifermin. One report describes a patient with multiple myeloma who developed intertriginous erythema and a papular eruption of the neck, trunk, and extremities 1 day after completing a 3-day course of palifermin.[2] In situ hybridization to test for human

Fig 1. Palifermin-associated papules. On the back of patient's forearms and hands were scattered 3- to 5-mm, flesh-colored, flat-topped papules without scale.

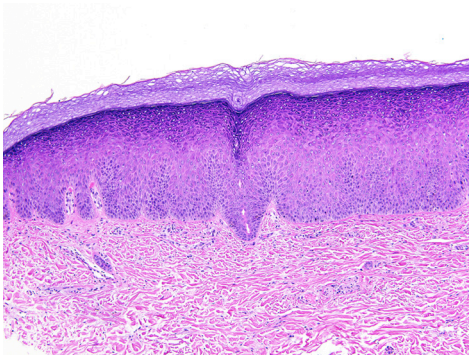

Fig 2. Palifermin-associated papules. Slightly mamillated epidermis with acanthosis, hypergranulosis, and mild keratinocytic atypia of the basal and lower spinous layers. (Hematoxylin-eosin stain; original magnification: ×100.)